



SEQUENCE LISTING

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<120> HEPARANASE ACTIVITY NEUTRALIZING ANTI-HEPARANASE MONOCLONAL ANTIBODY AND OTHER ANTI-HEPARANASE ANTIBODIES

<130> 30337

<160> 14

<170> PatentIn version 3.5

<210> 1
<211> 386
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> 45 kDa subunit of mature processed heparanase dimer

<400> 1

Lys Lys Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu
1 5 10 15

Tyr Thr Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn
20 25 30

Ala Leu Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln
35 40 45

Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu
50 55 60

Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile
65 70 75 80

Asn Gly Ser Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu
85 90 95

Arg Lys Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly
100 105 110

Gln Pro Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala
115 120 125

Gly Gly Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn
130 135 140

Gly Arg Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp

145 150 155 160
Ile Phe Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr
165 170 175

Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly
180 185 190

Gly Gly Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp
195 200 205

Leu Asp Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met
210 215 220

Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn
225 230 235 240

Phe Asp Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu
245 250 255

Val Gly Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg
260 265 270

Lys Leu Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr
275 280 285

Lys Glu Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr
290 295 300

Tyr Leu Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val
325 330 335

Gln Leu Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro
340 345 350

Pro Leu Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro
355 360 365

Ala Phe Ser Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala
370 375 380

Cys Ile
385

<210> 2
<211> 535
<212> PRT
<213> Mus musculus

<400> 2

Met Leu Arg Leu Leu Leu Trp Leu Trp Gly Pro Leu Gly Ala Leu

1 5 10 15

Ala Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp
20 25 30

Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe
35 40 45

Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu
50 55 60

Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser
65 70 75 80

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
85 90 95

Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser
100 105 110

Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val
115 120 125

Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu
130 135 140

Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser
145 150 155 160

Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu
165 170 175

Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn
180 185 190

Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr
195 200 205

Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys
210 215 220

Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu
225 230 235 240

Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr
245 250 255

Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg
260 265 270

Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His
275 280 285

His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser
290 295 300

Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys
305 310 315 320

Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr
325 330 335

Ser Ser Ala Tyr Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala
340 345 350

Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly
355 360 365

Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His
370 375 380

Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu
385 390 395 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys
405 410 415

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val
420 425 430

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn
435 440 445

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg
450 455 460

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu
465 470 475 480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp
485 490 495

Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser
500 505 510

Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn
515 520 525

Ala Lys Ile Ala Ala Cys Ile
530 535

<210> 3
<211> 536
<212> PRT
<213> Rattus norvegicus

<400> 3

Met Leu Arg Pro Leu Leu Leu Trp Leu Trp Gly Arg Leu Arg Ala
1 5 10 15

Leu Thr Gln Gly Thr Pro Ala Gly Thr Ala Pro Thr Lys Asp Val Val
20 25 30

Asp Leu Glu Phe Tyr Thr Lys Arg Leu Phe Gln Ser Val Ser Pro Ser
35 40 45

Phe Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe
50 55 60

Leu Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu
65 70 75 80

Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile
85 90 95

Phe Asp Pro Asn Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Gln
100 105 110

Ser Gln Asp Asn Asn Asp Ile Cys Gly Ser Glu Arg Val Ser Ala Asp
115 120 125

Val Leu Arg Lys Leu Gln Met Glu Trp Pro Phe Gln Glu Leu Leu
130 135 140

Leu Arg Glu Gln Tyr Gln Arg Glu Phe Lys Asn Ser Thr Tyr Ser Arg
145 150 155 160

Ser Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Arg Leu Asp
165 170 175

Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp
180 185 190

Asn Ser Ser Asn Ala Gln Leu Leu Asn Tyr Cys Ser Ser Lys Gly
195 200 205

Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys
210 215 220

Lys Ala Gln Ile Ser Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val
225 230 235 240

Glu Leu His Lys Leu Leu Gln Lys Ser Ala Phe Gln Asn Ala Lys Leu
245 250 255

Tyr Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu
260 265 270

Arg Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp
275 280 285

His His Tyr Tyr Leu Asn Gly Arg Val Ala Thr Lys Glu Asp Phe Leu
290 295 300

Ser Ser Asp Val Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu
305 310 315 320

Lys Val Thr Lys Glu Met Thr Pro Gly Lys Lys Val Trp Leu Gly Glu
325 330 335

Thr Ser Ser Ala Tyr Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe
340 345 350

Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Leu
355 360 365

Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr
370 375 380

His Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser
385 390 395 400

Leu Leu Phe Lys Lys Leu Val Gly Pro Lys Val Leu Met Ser Arg Val
405 410 415

Lys Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn
420 425 430

Val Tyr His Pro Arg Tyr Arg Glu Gly Asp Leu Thr Leu Tyr Val Leu
435 440 445

Asn Leu His Asn Val Thr Lys His Leu Lys Leu Pro Pro Pro Met Phe
450 455 460

Ser Arg Pro Val Asp Lys Tyr Leu Leu Lys Pro Phe Gly Ser Asp Gly
465 470 475 480

Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Thr Leu Lys Met Val
485 490 495

Asp Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly
500 505 510

Ser Ser Leu Ser Val Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg
515 520 525

Asn Ala Lys Ile Ala Ala Cys Ile
530 535

<210> 4
<211> 543
<212> PRT
<213> Homo sapiens

<400> 4

Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu Leu
1 5 10 15

Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro
20 25 30

Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
35 40 45

Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
50 55 60

Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
65 70 75 80

Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
85 90 95

Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
100 105 110

Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys
115 120 125

Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
130 135 140

Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
145 150 155 160

Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
165 170 175

Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
180 185 190

Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
195 200 205

Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn
210 215 220

Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser
225 230 235 240

Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser
245 250 255

Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
260 265 270

Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
275 280 285

Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
290 295 300

Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
305 310 315 320

Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly
325 330 335

Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Ala
340 345 350

Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys
355 360 365

Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val
370 375 380

Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro
385 390 395 400

Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
405 410 415

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
420 425 430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
435 440 445

Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
450 455 460

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu
465 470 475 480

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn
485 490 495

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met
500 505 510

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
515 520 525

Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
530 535 540

<210> 5
<211> 523
<212> PRT
<213> Gallus gallus

<400> 5

Met Leu Val Leu Leu Leu Val Leu Leu Ala Val Pro Pro Arg
1 5 10 15

Arg Thr Ala Glu Leu Gln Leu Gly Leu Arg Glu Pro Ile Gly Ala Val
20 25 30

Ser Pro Ala Phe Leu Ser Leu Thr Leu Asp Ala Ser Leu Ala Arg Asp
35 40 45

Pro Arg Phe Val Ala Leu Leu Arg His Pro Lys Leu His Thr Leu Ala
50 55 60

Ser Gly Leu Ser Pro Gly Phe Leu Arg Phe Gly Gly Thr Ser Thr Asp
65 70 75 80

Phe Leu Ile Phe Asn Pro Asn Lys Asp Ser Thr Trp Glu Glu Lys Val
85 90 95

Leu Ser Glu Phe Gln Ala Lys Asp Val Cys Glu Ala Trp Pro Ser Phe
100 105 110

Ala Val Val Pro Lys Leu Leu Leu Thr Gln Trp Pro Leu Gln Glu Lys
115 120 125

Leu Leu Leu Ala Glu His Ser Trp Lys Lys His Lys Asn Thr Thr Ile
130 135 140

Thr Arg Ser Thr Leu Asp Ile Leu His Thr Phe Ala Ser Ser Ser Gly
145 150 155 160

Phe Arg Leu Val Phe Gly Leu Asn Ala Leu Leu Arg Arg Ala Gly Leu
165 170 175

Gln Trp Asp Ser Ser Asn Ala Lys Gln Leu Leu Gly Tyr Cys Ala Gln
180 185 190

Arg Ser Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe
195 200 205

Arg Lys Lys Ser Gly Ile Cys Ile Asp Gly Phe Gln Leu Gly Arg Asp
210 215 220

Phe Val His Leu Arg Gln Leu Leu Ser Gln His Pro Leu Tyr Arg His
225 230 235 240

Ala Glu Leu Tyr Gly Leu Asp Val Gly Gln Pro Arg Lys His Thr Gln
245 250 255

His Leu Leu Arg Ser Phe Met Lys Ser Gly Gly Lys Ala Ile Asp Ser
260 265 270

Val Thr Trp His His Tyr Tyr Val Asn Gly Arg Ser Ala Thr Arg Glu

275

280

285

Asp Phe Leu Ser Pro Glu Val Leu Asp Ser Phe Ala Thr Ala Ile His
290 295 300

Asp Val Leu Gly Ile Val Glu Ala Thr Val Pro Gly Lys Lys Val Trp
305 310 315 320

Leu Gly Glu Thr Gly Ser Ala Tyr Gly Gly Ala Pro Gln Leu Ser
325 330 335

Asn Thr Tyr Val Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ala
340 345 350

Ala Arg Arg Gly Ile Asp Val Val Met Arg Gln Val Ser Phe Gly Ala
355 360 365

Gly Ser Tyr His Leu Val Asp Ala Gly Phe Lys Pro Leu Pro Asp Tyr
370 375 380

Trp Leu Ser Leu Leu Tyr Lys Arg Leu Val Gly Thr Arg Val Leu Gln
385 390 395 400

Ala Ser Val Glu Gln Ala Asp Ala Arg Arg Pro Arg Val Tyr Leu His
405 410 415

Cys Thr Asn Pro Arg His Pro Lys Tyr Arg Glu Gly Asp Val Thr Leu
420 425 430

Phe Ala Leu Asn Leu Ser Asn Val Thr Gln Ser Leu Gln Leu Pro Lys
435 440 445

Gln Leu Trp Ser Lys Ser Val Asp Gln Tyr Leu Leu Leu Pro His Gly
450 455 460

Lys Asp Ser Ile Leu Ser Arg Glu Val Gln Leu Asn Gly Arg Leu Leu
465 470 475 480

Gln Met Val Asp Asp Glu Thr Leu Pro Ala Leu His Glu Met Ala Leu
485 490 495

Ala Pro Gly Ser Thr Leu Gly Leu Pro Ala Phe Ser Tyr Gly Phe Tyr
500 505 510

Val Ile Arg Asn Ala Lys Ala Ile Ala Cys Ile
515 520

<210> 6
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> Functional peptide epitope of heparanase

<400> 6

Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys
1 5 10

<210> 7

<211> 19

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 7

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
1 5 10 15

Asp Pro Lys

<210> 8

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 8

Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala
1 5 10 15

<210> 9

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 9

Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr
1 5 10 15

<210> 10

<211> 14

<212> PRT

<213> Artificial sequence

<220>

<223> Functional peptide epitope of heparanase

<400> 10

Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg
1 5 10

<210> 11

<211> 74

<212> PRT

<213> Homo sapiens

<220>
<221> misc_feature
<223> 8 kDa subunit of mature processed heparanase dimer
<400> 11

Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His Leu
1 5 10 15

Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr
20 25 30

Asp Pro Arg Phe Leu Ile Leu Gly Ser Pro Lys Leu Arg Thr Leu
35 40 45

Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr
50 55 60

Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu
65 70

<210> 12
<211> 6
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> A conserved basic amino acid cluster (residues 157-162 of the
human heparanase)

<400> 12

Gln Lys Lys Phe Lys Asn
1 5

<210> 13
<211> 8
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> A conserved basic amino acid cluster (residues 271-278 of the
human heparanase)

<400> 13

Pro Arg Arg Lys Thr Ala Lys Met
1 5

<210> 14
<211> 8
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> A conserved basic amino acid cluster (residues 426-433 of the
human heparanase)

<400> 14

Ser Lys Arg Arg Lys Leu Arg Val
1 5